

June 30, 2008

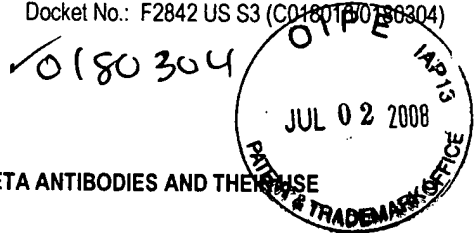
Docket No.: F2842 US S3 (C0180150786304)

In re Patent Application of :
Michael BARDROFF *et al.*

Serial No.: 10/505,313

Filed: August 20, 2004

For: ANTI-AMYLOID BETA ANTIBODIES AND THEIR USE



Enclosed:

1/ Response To Office Action Including Amendment and Request For Extension of Time with certificate of mailing (27 pp, incl. duplicate pg. 1); with Exhibits 1 & 2

Exhibit 1: Substitute Sequence List (200 pages)

Exhibit 2: Substitute Sequence List in CRF (1 diskette)

2. \$460.00 check to cover two-month extension; and

3. Return Postcard

PLEASE DATE STAMP AND RETURN TO ACKNOWLEDGE RECEIPT

✓ Lang: mh



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,313	03/07/2005	Michael Bardroff	F2842 US S3 (C018016/0180)	1924
7590 07/28/2008				
Stephen M Haracz Bryan Cave 1290 Avenue of the Americas New York, NY 10104-3300			EXAMINER EMCH, GREGORY S	
			ART UNIT 1649	PAPER NUMBER
			MAIL DATE 07/28/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Interview Summary

Application No.

10/505,313

Applicant(s)

BARDROFF ET AL.

Examiner

Gregory S. Emch

Art Unit

1649

All participants (applicant, applicant's representative, PTO personnel):

(1) Gregory S. Emch.(3) Stephen Haracz.(2) Elizabeth Kemmerer.(4) Jihong Zang.

Date of Interview: 09 July 2008.

Type: a) ☒ Telephonic b) ☐ Video Conference
c) ☐ Personal [copy given to: 1) ☐ applicant 2) ☐ applicant's representative]

Exhibit shown or demonstration conducted: d) ☐ Yes e) ☐ No.
If Yes, brief description: _____.

Claim(s) discussed: 1-9, 11-16, 22, 29, 30 and 41-49.

Identification of prior art discussed: None.

Agreement with respect to the claims f) ☐ was reached. g) ☒ was not reached. h) ☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: Participants discussed the claim amendments submitted in the reply filed on 02 July 2008. The examiners informed applicants' representatives that it is unclear how the newly submitted claim amendments read on the elected invention. It was proposed that Applicants' representatives submit a subsequent response to address this issue. Participants also discussed the rejection of claim 7 under 35 U.S.C. 112, first paragraph.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

/Gregory S. Emch/

Examiner Note: You must sign this form unless it is an
Attachment to a signed Office action.

Examiner's signature, if required



Docket No.: F2842 US S3 (C018016/0180304)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)

Michael BARDROFF *et al.*)

Examiner: G. S. Emch

Serial No.: 10/505,313)

Art Unit: 1649

Filed: August 20, 2004)

For: **ANTI-AMYLOID BETA ANTIBODIES
AND THEIR USE**

New York, New York
July 24, 2008

**SUPPLEMENTAL RESPONSE TO OFFICE ACTION,
INCLUDING SUMMARY OF EXAMINER'S INTERVIEW,
AMENDMENT AND REQUEST FOR EXTENSION OF TIME**

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is a supplemental response to the Non-Final Office Action mailed January 28, 2008, which set a three-month shortened statutory period for response. Accordingly, this response is filed timely upon mailing, with an executed certificate of mailing, on or before July 28, 2008, with a three-month extension. 37 CFR §§ 1.8 and 1.136.

As a two-month extension of time to respond to the Office Action was previously requested and paid for, an additional (third) month extension is hereby requested. Enclosed is a check in the amount of \$590.00 (\$1050 - \$460 previously paid) to cover the third month. Please charge any required extension-of-time fees, or any other fees, not otherwise paid by check to Deposit Account No. 02-4467. A duplicate copy of this sheet is enclosed.

This response is filed in view of the helpful comments and suggestions offered by Examiners Emch and Kemmerer during a telephonic interview with undersigned counsel on July 8, 2008. During the interview, the Examiners noted the restriction requirement and the search requirements implicated by the previously amended claims and requested additional amendments and/or remarks to facilitate examination of the elected subject matter. The Examiners also asked for additional comments regarding how claims 41-49 read on the elected subject matter. In addition, the enablement rejection with respect to claim 7 was discussed and further comments were requested concerning applicants' position as regard to the lack of need for deposit of MSR-7.

The issues raised during the interview are addressed below via further claim amendments and additional remarks.

Please amend the application as follows:

AMENDMENTS TO THE SPECIFICATION: None.

AMENDMENTS TO THE CLAIMS are reflected in the listing of claims, which begins on page 3 of this paper.

REMARKS begin on page 9 of this paper.



AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

LISTING OF CLAIMS:

Claim 1. (Currently Amended) An antibody molecule capable of specifically recognizing two regions of the β -A4 peptide/A β 4, wherein the first region comprises the amino acid sequence AEFRHDSGY as shown in SEQ ID NO: 1 or a fragment thereof and wherein the second region comprises the amino acid sequence VHHQKLVFFAEDVG as shown in SEQ ID NO: 2 or a fragment thereof, wherein said antibody molecule comprises

(a) a variable V_L-Region comprising complementary determining regions, L-CDR1, L-CDR2, L-CDR3, wherein:

- (1) L-CDR1 comprises a sequence selected from the group consisting of
SEQ ID NOs: 96, 160, 175-177, 180, 189-190, 200-201, and 206-
210~~96, 130-133, 141-143, 160, 175-177, 180, 189, 190, 200, 201,~~
~~206-211, and 224;~~
- (2) L-CDR2 comprises a sequence selected from the group consisting of
SEQ ID NOs: 97 and 161 ~~97, 144, 161, and 212;~~ and
- (3) L-CDR3 comprises a sequence selected from the group consisting of
SEQ ID NOs: 18, 79, 81, 95, 149, 151-156, 158-159 and 166~~16,~~
~~18, 20, 75, 77, 79, 81, 83, 85, 87, 95, 98, 102, 103-107, 145, 149-~~
~~159, 162, 166, 178, 183, 202, 213, 217, 218, 220, 385, 387, 389,~~

~~391, 393, 395, 397, 399, 401, 403, 405, 407, 409, 411 and 413;~~

and

(b) a variable V_H-Region comprising complementary determining regions, H-CDR1, H-CDR2, H-CDR3, wherein:

(1) H-CDR1 comprises a sequence selected from the group consisting of

SEQ ID NOs: 99 and 16399, 146, 163, 203, and 214;

(2) H-CDR2 comprises a sequence selected from the group consisting of

SEQ ID NOs: 100, 164, 167-169, 170-174, 179, 181-182, 184-188,

192-197, 199 and 204 ~~100, 108-129, 134-140, 147, 164, 167-174,~~

~~179, 181, 182, 184-188, 191-199, 204, 205, 215, 219, and 221-~~

~~223;~~ and

(3) H-CDR3 comprises a sequence selected from the group consisting of

SEQ ID NO: 24. ~~NOs: 22, 24, 26, 61, 63, 65, 67, 69, 71, 73, 93,~~

~~101, 148, 165, 216, 355, 357, 359, 361, 363, 365, 367, 369, 371,~~

~~373, 375, 377, 379, 381, and 383.~~

Claim 2. (Original) The antibody molecule of claim 1, wherein said antibody molecule recognizes at least two consecutive amino acids within the two regions of β -A4.

Claim 3. (Previously Presented) The antibody molecule of claim 1, wherein said antibody molecule recognizes in the first region an amino acid sequence selected from the group consisting of EF, EFR, FR, and SEQ ID NOs: 415 – 418, and in the second region an amino acid sequence selected from the group consisting of LV and SEQ ID NOs: 419 - 423.

Claim 4. (Currently Amended) The antibody molecule of claim 1, wherein said antibody molecule comprises a variable V_H-region comprising a sequence selected from the group consisting of SEQ ID NOs: 6, 37, 39, 41, 43, 89, and 425. ~~as encoded by a nucleic acid molecule as shown in a SEQ ID NO selected from the group consisting of SEQ ID NOs: 3, 5 and 7, or a variable V_H-region as shown in a SEQ ID NO: selected from the group consisting of SEQ ID NOs: 4, 6 and 8.~~

Claim 5. (Currently Amended) The antibody molecule of claim 1, wherein said antibody molecule comprises a variable V_L-region comprising a sequence selected from the group consisting of SEQ ID NOs: 12, 51, 53, 57, and 91. ~~as encoded by a nucleic acid molecule as shown in a SEQ ID NO selected from the group consisting of SEQ ID NOs: 9, 11 and 13, or a variable V_L-region as shown in a SEQ ID NO selected from the group consisting of SEQ ID NOs: 10, 12 and 14.~~

Claim 6. (Cancelled).

Claim 7. (Currently Amended) The antibody molecule of claim 1, wherein said antibody is selected from the group consisting of MSR-7 ~~MSR-3, 7 and 8~~, and an affinity-matured version of MSR-7 ~~MSR-3, 7 and 8~~.

Claim 8. (Previously Presented) The antibody molecule of claim 1, wherein said antibody molecule is a full antibody (immunoglobulin), a F(ab)-fragment, a F(ab)₂-fragment, a single-chain antibody, a chimeric antibody, a CDR-grafted antibody, a bivalent antibody-construct, a synthetic antibody or a cross-cloned antibody.

Claim 9. (Previously Presented) The antibody molecule of claim 1, wherein said two regions of β -A4 form a conformational epitope or a discontinuous epitope.

Claim 10. (Cancelled).

Claim 11. (Previously Presented) A nucleic acid molecule encoding an antibody molecule according to claim 1.

Claim 12. (Original) A vector comprising the nucleic acid molecule of claim 11.

Claim 13. (Original) A host cell comprising the vector of claim 12.

Claim 14. (Previously Presented) A method for the preparation of an antibody molecule comprising culturing the host cell of claim 13 under conditions that allow synthesis of said antibody molecule and recovering said antibody molecule from said culture.

Claim 15. (Previously Presented) A pharmaceutical or diagnostic composition comprising an antibody molecule according to claim 1 and a carrier or diluent.

Claim 16. (Previously Presented) The composition of claim 15, which is a pharmaceutical composition.

Claims 17-21. (Cancelled).

Claim 22. (Previously Presented) A kit comprising an antibody molecule according to claim 1, a nucleic acid molecule according to claim 11, a vector according to claim 12 or a host cell according to claim 13, wherein the antibody, nucleic acid, vector or host cell is contained in at least one vial, bottle, container or multicontainer unit.

Claims 23-28. (Cancelled).

Claim 29. (Previously Presented) A composition comprising an antibody molecule produced by the method of claim 14.

Claim 30. (Previously Presented) The composition of claim 16 further comprising a pharmaceutically acceptable carrier and/or diluent.

Claims 31-40. (Cancelled).

Claim 41. (Previously Presented) An antibody molecule comprising

(a) a variable V_L -Region comprising complementary determining regions, L-CDR1, L-CDR2, L-CDR3, wherein:

(1) L-CDR1 comprises SEQ ID NO: 143;

(2) L-CDR2 comprises SEQ ID NO: 144; and

(3) L-CDR3 comprises SEQ ID NO: 95; and

(b) a variable V_H -Region comprising complementary determining regions, H-CDR1, H-CDR2, H-CDR3, wherein:

(1) H-CDR1 comprises SEQ ID NO: 146;

(2) H-CDR2 comprises SEQ ID NOs: 192; and

(3) H-CDR3 comprises SEQ ID NOs: 93.

Claim 42. (Previously Presented) The antibody molecule according to claim 41, wherein the antibody is of the IgG1 subtype.

Claim 43. (Previously Presented) The antibody molecule according to claim 41, wherein the variable V_H -region comprises SEQ ID NO: 89; and the variable V_L -region comprises SEQ ID NO: 91.

Claim 44. (Previously Presented) The antibody molecule according to claim 43, wherein the antibody is of the IgG1 subtype.

Claim 45. (Previously Presented) The antibody molecule according to claim 41, wherein the variable V_H -region comprises SEQ ID NO: 425; and the variable V_L -region comprises SEQ ID NO: 91.

Claim 46. (Previously Presented) The antibody molecule according to claim 45, wherein the antibody is of the IgG1 subtype.

Claim 47. (Previously Presented) A pharmaceutical composition comprising an antibody molecule according to claim 41 and a pharmaceutically acceptable carrier or diluent.

Claim 48. (Previously Presented) A pharmaceutical composition comprising an antibody molecule according to claim 44 and a pharmaceutically acceptable carrier or diluent.

Claim 49. (Previously Presented) A pharmaceutical composition comprising an antibody molecule according to claim 46 and a pharmaceutically acceptable carrier or diluent.

REMARKS

Amendments to the Claims

Claim 1 has been further amended to omit subject matter related to MSR-3 and MSR-8 and to instead recite only subject matter related to MSR-7, the elected species.

In particular, claim 1 now recites that the antibody molecules comprise CDRs of the MSR-7 antibody and the affinity-matured versions thereof described in Table 1. The SEQ ID NOs recited in claim 1 correspond only to the CDR amino acid sequences of MSR-7 antibody and the affinity-matured versions thereof listed in Table 1. The portion of Table 1 listing the CDR sequences of such MSR-7 antibody and the affinity-matured versions, as well as the corresponding SEQ ID NOs. of such sequences, are shown in the attached Exhibit 1.

The Examiner will note that there is only one sequence for H-CDR3, and that there are only two sequences for each of H-CDR1 and L-CDR2. This redundancy, along with the deletion of CDR sequences relating to MSR-3 and MSR-8, should facilitate search and examination, as the Examiners requested.

Support for the amendment to claim 1 may be found in Table 1 at pages 64-68, and see also the specification at, for example, page 15, lines 3-15; page 16, lines 18-29; page 20, lines 1-18. See also the original Sequence Listing as filed; and the Substitute Sequence Listing.

Claim 4 has been amended to omit subject matter related to MSR-3 and MSR-8. As amended, claim 4 recites specific heavy chain variable sequences that include H-CDRs of MSR-7 antibody or certain affinity-matured versions thereof. The

Examiner will note that the framework regions surrounding the CDRs are included in the recited sequences. The table below sets forth the SEQ ID No. of each of the three H-CDRs contained within the variable heavy chain sequences now recited in claim 4; SEQ ID NO: 6 is the sequence for the variable heavy chain of MSR-7.

SEQ ID NO.	H-CDR1 SEQ ID NO.	H-CDR2 SEQ ID NO.	H-CDR3 SEQ ID NO.
6	99	100	24
37	99	182	24
39	99	185	24
41	99	187	24
43	99	195	24
89	99	192	24
425	99	192	24

Support for the amendment to claim 4 may be found in original claim 4 and in the specification at, for example, page 14, lines 9-30; page 18, lines 6-15; the original Sequence Listing as filed, and the Substitute Sequence Listing. See *In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l).

A conforming amendment has also been made to claim 5 in order to delete subject matter related to MSR-3 and MSR-8. Claim 5 as amended recites specific light chain variable sequences that include L-CDRs of MSR-7 antibody or certain affinity-matured versions thereof. The Examiner will note that the framework regions are included in such variable light chain sequences. The table below sets forth the SEQ ID No. of each of the three L-CDRs contained within the variable light chain sequences now recited in claim 5; SEQ ID No: 12 is the sequence for the variable light of MSR-7.

SEQ ID No.	L-CDR1 SEQ ID NO.	L-CDR2 SEQ ID NO.	L-CDR3 SEQ ID NO.
12	96	97	18
51	175	97	79
53	206	161	81
57	200	97	159
91	96	97	95

Support for the amendment to claim 5 may be found in original claim 5 and in the specification at, for example, page 14, lines 9-30; page 18, lines 6-15; the original Sequence Listing as filed, and the Substitute Sequence Listing. *Id.*

Claim 7 has been amended to omit subject matter related to MSR-3 and MSR-8, reciting only the MSR-7 antibody and affinity-matured versions thereof. Support for this amendment may be found in original claim 7. *Id.*

It is submitted that no new matter has been introduced by the foregoing amendments.

Claims 41-49

With respect to the Examiners' request for supplemental comments regarding how claims 41-49 read on the elected MSR-7 species, the six CDRs recited in claim 41 are taken from the family of MSR-7 CDRs that are now recited in independent claim 1. See discussion above explaining how claim 1 has been amended to recite only CDRs of the elected MSR-7 family, omitting the MSR-3 and MSR-8 families. More particularly, claims 41-49 recite the six CDRs of "MSR-7.9 H7," a particular affinity-matured derivative of MSR-7. See Table 1 at page 67.

Claim 43 recites the complete variable heavy region (SEQ ID NO:89) and the complete variable light region (SEQ ID NO: 91) of MSR-7.9 H7. See Table 10 at

page 98. The structure embraced by claim 43 thus includes the six CDRs recited in claim 41 and also includes the adjacent framework residues contained within the specified variable regions.

As noted in the Response dated June 30, 2008, claim 45 recites the same variable light region (SEQ ID NO: 91) as claim 43, but recites a slightly different variable heavy region (SEQ ID NO: 425). As previously noted, SEQ ID NO: 425 differs from SEQ ID NO: 89 in that the third residue of SEQ ID NO: 425 is "E" rather than "Q." This difference is in the framework residues and not in any of the six CDRs commonly embraced by claims 41-49.

In summary, it is believed that claims 41-49, directed to two closely related affinity matured relatives of MSR-7, read on and are consistent with the elected subject matter. Should the Examiner's be of a different view, it is respectfully requested that the subject matter of claim 41 be treated as a single elected species for purposes of the restriction requirement and initial search and examination of the amended claims.

Enablement Rejection – Claim 7

Claim 7 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. (Paper No. 20080117 at 6). In making the rejection, the Examiner asserted that "[t]he invention appears to employ novel biological materials, specifically the MSR-3, MSR-7 and MSR-8 antibodies." (*Id.* at 7.) The Examiner further asserted that "[s]ince the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public." (*Id.*) In addition, the Examiner asserted, "[t]he specification does not disclose a repeatable process to

obtain the biological materials and it is not apparent if the biological materials are readily available to the public." (*Id.*)

The rejection is respectfully traversed. The applicants submit the following reasons in addition to the reasons set forth in the Response dated June 30, 2008.

Initially, we note that claim 7 has been amended to delete MSR-3 and MSR-8.

We also note that the Examiner has expressly acknowledged that the specification is "enabling for antibodies or fragments thereof that comprise 6 CDRs, three from the [V_H] domain and three from the [V_L] domain." (Paper No. 20080117 at 4). With regard to MSR-7, the specification lists all 6 CDRs for MSR-7 and for affinity matured versions thereof (see, e.g., Table 1, pages 64-68). In view of the Examiner's acknowledgment that the disclosed CDR sequences enable one to make and use the claimed antibodies, including MSR-7, it is respectfully submitted that no deposit of MSR-7 is needed.

Indeed, Table 10 sets forth the SEQ ID NOs of amino acid sequences of the full variable regions of MSR-7, as well as the DNA sequence encoding such amino acid sequences (page 98). SEQ ID NOs: 5 and 6 are the encoding DNA and amino acid sequences, respectively, of the V_H-region of MSR-7. SEQ ID NOs: 11 and 12 correspond to the encoding DNA sequence and the amino acid sequences of the V_L-region of MSR-7, respectively. The variable heavy and light sequences include not only the CDRs, but also the framework amino acids surrounding the CDRs.

In view of the Examiner's acknowledgement, and in view of the reasons set forth above and in the Response dated June 30, 2008, it is respectfully submitted that the enablement rejection of claim 7 should be withdrawn. The specification describes not only the six CDRs of MSR-7, but also the amino acid sequence of the complete variable heavy and light chains of MSR-7. The specification also describes encoding DNA sequences for both the six CDRs of MSR-7 and the complete variable heavy and light chains of MSR-7.

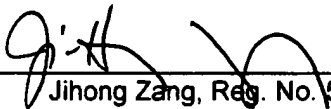
Given the description of the complete structure, there is no need for a cell line that makes that structure. To conclude otherwise would require deposit of every specific embodiment for which CDRs and variable sequences are provided, which is not a requirement under § 112, first paragraph.

Reconsideration and withdrawal of the enablement rejection of claim 7 is respectfully requested.

Application No.: 10/505,313
Amendment Dated: July 24, 2008
Reply to Non-Final Office Action: January 28, 2008

For the reasons set forth above, entry of the amendments and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on July 24, 2008.



Jihong Zang, Reg. No. 56,606

Respectfully submitted,

By: 

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Name	L-CDR1	SEQ ID NO.	L-CDR2	SEQ ID NO.	L-CDR3	SEQ ID NO.	H-CDR1	SEQ ID NO.	H-CDR2	SEQ ID NO.	H-CDR3	SEQ ID NO.
MS-Roché #7	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	FOLYSDPF	18, 145	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	100, 147, 215	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.1	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	HOLYSSPY	149	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	100, 147, 215	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.2	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	QOIVSFPH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	100, 147, 215	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.3	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	HQVYSHPF	151, 178	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	100, 147, 215	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.4	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	QOIVNFPH	152	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	100, 147, 215	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.5	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	HQVYSSPF	153	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	100, 147, 215	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.6	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	HOLYSSPY	154	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	100, 147, 215	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.7	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	HQVYSAFP	155	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	100, 147, 215	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.8	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	HQVYSFPI	156	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	100, 147, 215	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.9	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	LOIYNMFI	95, 157, 183, 409	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	100, 147, 215	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.10	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	QOIVNPPH	158	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	100, 147, 215	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.11	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	QOIVSPPH	159	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	100, 147, 215	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.12	RASQSVSSSYLA	160	GSSNRAT	97, 144, 212	LOIYNIPN	81, 83, 162, 202, 401, 405, 411	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	164, 205	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.13	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	HQVYSPPF	166	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	100, 147, 215	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.2.H1	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	QOIVSFPH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	167	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.2.H2	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	QOIVSFPH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	168	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.2.H3	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	QOIVSFPH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	169, 198	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.2.H4	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	QOIVSFPH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	170	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.2.H5	RASQSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	QOIVSFPH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AISGGSGSTYYADSVKVG	171	GKGNTHKPYGVYRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381

MS-Roché #7.2.H8	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QIYSPFH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AINARGNRTYYADSVKG	172	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.2.H7	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QIYSPFH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AINSGSDTHYADSVKG	173	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.2.H8	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QIYSPFH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AINASGHKTYADSVKG	174	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.2.L1	RASQVVDRTYLA	175	GASSRAT	97, 144, 212	QIYSPFH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AINSGSGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.3.H1	RASQVYSFYLA	176	GASSRAT	97, 144, 212	QIYSPFH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AINSGSGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.2.L4	RASQVIRRSYLA	177	GASSRAT	97, 144, 212	QIYSPFH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AINSGSGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.3.H1	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QIYSPFH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AINSGSGSTYYADSVKG	179	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.3.L1	RASQVLYGYLA	180	GASSRAT	97, 144, 212	QIYSPFH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AINSGSGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.4.H1	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QIYSPFH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AINATGYRTYYADSVKG	181	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.4.H2	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QIYSPFH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AINYNGARIYYADSVKG	182	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.8.H1	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LOIYNMFI	95, 157, 183, 409	GTFSSYAMS	99, 146, 214	AINANGORFYADSVKG	184	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.8.H2	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LOIYNMFI	95, 157, 183, 409	GTFSSYAMS	99, 146, 214	AINADGNRKYADSVKG	185	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.8.H3	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LOIYNMFI	95, 157, 183, 409	GTFSSYAMS	99, 146, 214	AINYQGNRKYADSVKG	186	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.8.H4	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LOIYNMFI	95, 157, 183, 409	GTFSSYAMS	99, 146, 214	AINAVGMKKFYADSVKG	187	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.8.H5	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LOIYNMFI	95, 157, 183, 409	GTFSSYAMS	99, 146, 214	AINHAGNKKYYADSVKG	188	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.8.L1	RASQRLSPRYLA	189	GASSRAT	97, 144, 212	LOIYNMFI	95, 157, 183, 409	GTFSSYAMS	99, 146, 214	AINSGSGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.8.L2	RASQVLYKRYLA	190	GASSRAT	97, 144, 212	LOIYNMFI	95, 157, 183, 409	GTFSSYAMS	99, 146, 214	AINSGSGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.8.H8	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QIYSPFH	79, 87, 150, 399, 403, 407	GTFSSYAMS	99, 146, 214	AINARGNRTYYADSVKG	172	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roché #7.8.H7	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LOIYNMFI	95, 157, 183, 409	GTFSSYAMS	99, 146, 214	AINASGTRTYADSVKG	192	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381

MS-Rocha #7.9.H8	RASOSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	LQYNMIP	95, 157, 183, 409	GTFSSYAMS	99, 146, 214	AINAGSKYYADSVKG	193	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha #7.9.H9	RASOSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	LQYNMIP	95, 157, 183, 409	GTFSSYAMS	99, 146, 214	AINAGKNNYYADSVKG	194	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha #7.11.H1	RASOSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	QQVYSPPH	159	GTFSSYAMS	99, 146, 214	GINAAGFRYYADSVKG	195	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha #7.11.H2	RASOSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	QQVYSPPH	159	GTFSSYAMS	99, 146, 214	AINANGYKYYADSVKG	196	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha #7.11.H3	RASOSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	QQVYSPPH	159	GTFSSYAMS	99, 146, 214	GINANGNRYYADSVKG	197	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha #7.11.H4	RASOSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	QQVYSPPH	159	GTFSSYAMS	99, 146, 214	AINANGYKYYADSVKG	169, 198	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha #7.11.H5	RASOSVSSSYLA	98, 143, 211	GASSRAT	97, 144, 212	QQVYSPPH	159	GTFSSYAMS	99, 146, 214	AINANGQRTYYADSVKG	199	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha # 7.11.L1	RASORLRYLA	200	GASSRAT	97, 144, 212	QQVYSPPH	159	GTFSSYAMS	99, 146, 214	AINSGSGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha #7.12.H1	RASOYVFRYYLA	201	GSSNRAT	161	LQYNIPN	81, 83, 162, 202, 401, 405, 411	GTFSSYGMS	163, 203	NINGNKNRYYADSVKG	204	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha #7.12.L1	RASOYVFRYYLA	201	GSSNRAT	161	LQYNIPN	81, 83, 162, 202, 401, 405, 411	GTFSSYGMS	163, 203	NISGSGSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha #7.12.L2	RASORFFYYLA	208	GSSNRAT	161	LQYNIPN	81, 83, 162, 202, 401, 405, 411	GTFSSYGMS	163, 203	NISGSGSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha #7.12.L3	RASOFVRRGFLA	207	GSSNRAT	161	LQYNIPN	81, 83, 162, 202, 401, 405, 411	GTFSSYGMS	163, 203	NISGSGSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha #7.12.L4	RASORLKRYYLA	208	GSSNRAT	161	LQYNIPN	81, 83, 162, 202, 401, 405, 411	GTFSSYGMS	163, 203	NISGSGSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha #7.12.L5	RASORLKRYYLA	208	GSSNRAT	161	LQYNIPN	81, 83, 162, 202, 401, 405, 411	GTFSSYGMS	163, 203	NISGSGSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha #7.12.L6	RASOYLWRYLA	209	GSSNRAT	161	LQYNIPN	81, 83, 162, 202, 401, 405, 411	GTFSSYGMS	163, 203	NISGSGSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Rocha #7.12.L7	RASOWIRKTYLA	210	GSSNRAT	161	LQYNIPN	81, 83, 162, 202, 401, 405, 411	GTFSSYGMS	163, 203	NISGSGSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381